Towards Complex Matter
From Supramolecular Chemistry to Adaptive Chemistry

Jean-Marie Lehn
The Big Bang

PHYSICS

CHEMISTRY

BIOLOGY

Chemistry starts around here

Life on Earth

Thought

13.7 billion years

Life on Earth

Thought

Thought
EVOLUTION of the UNIVERSE

EVOLUTION towards COMPLEX MATTER

EVOLUTION of MATTER under the PRESSURE of INFORMATION
How has matter become complex in the history of the universe up to the evolution of the biological world? What higher forms of complex matter are here to be evolved, to be created?

Basic Question: How does matter become complex from the elementary particle to the thinking organism?

Physics

Chemistry

Biology

The Bridge towards Complex Matter
SELF-ORGANIZATION

THE PATH TOWARDS COMPLEX MATTER

DIVIDED – CONDENSED - ORGANIZED
LIVING – THINKING MATTER !
PREBIOTIC CHEMICAL EVOLUTION

SELF-ORGANIZATION of
NON-LIVING MOLECULAR MATTER

Electromagnetic forces operate selection on structural diversity leading to the progressive complexification of matter from the non-living to the living world under the pressure of information.

GENERALIZATION of
DARWINIAN EVOLUTION

Chemical evolution through selection on structural diversity driven by intra and intermolecular forces implementing molecular information.
EMERGENCE of COMPLEX ENTITIES

SELF-ORGANIZATION
operating on
RANDOM DIVERSITY

Structuration of molecular matter by the electromagnetic forces generating and operating on random structural combinations
CHEMISTRY

The SCIENCE of the

STRUCTURE and

TRANSFORMATION of NON-LIVING and LIVING MATTER
Mastering the Organization of Molecular Matter
Building highly complex molecules from atoms linked by **covalent bonds**

**MOLECULAR CHEMISTRY**

From the **ATOM** to the **MOLECULE**
MILESTONES in MOLECULAR CHEMISTRY

UREA

\[
\begin{align*}
H_2N & \quad \text{CON} & \quad \text{NH}_2 \\
\text{1828} & & \\
\text{Friedrich Wöhler}
\end{align*}
\]

VITAMIN B$_{12}$

\[
\begin{align*}
\text{1972(1976)} & \\
\text{Robert Woodward} & \\
\text{Albert Eschenmoser}
\end{align*}
\]
A CANCER CELL and TWO KILLER CELLS

WHITE BLOOD CELL and PARTICLES of the HIV VIRUS
Implementing the interactions between molecules
CHEMISTRY BEYOND THE MOLECULE
SUPRAMOLECULAR CHEMISTRY

TO

FROM
MOLECULAR CHEMISTRY
SUPRAMOLECULAR CHEMISTRY

CHEMISTRY BEYOND THE COVALENT BOND
Mastering the NON-COVALENT BOND

☆ CHEMISTRY of the ENTITIES
   linked by INTERMOLECULAR INTERACTIONS

☆ CHEMISTRY of SYSTEMS based on
   CHEMISTRY of SPECIES and INTERACTIONS

⇒ RECOGNITION, REACTIVITY and TRANSPORT
  (CATALYSIS)
INTERMOLECULAR INTERACTIONS
for
SUPRAMOLECULAR CHEMISTRY

- Electrostatic Interactions
- Hydrogen Bonding
- Donor-Acceptor Interactions
- Van der Waals Forces
- Metal Ion Coordination

+ Medium effects: solvophobic
MOLECULAR RECOGNITION

requires INTERACTION for BINDING

INFORMATION for SELECTING

DOUBLE COMPLEMENTARITY \{ geometrical interactional \}

PREORGANIZATION

“SCHLOSS und SCHLÜSSEL”
LOCK and KEY

Emil FISCHER 1894
CHEMISTRY : an INFORMATION SCIENCE

The SCIENCE of INFORMED MATTER

MOLECULAR STORAGE

SUPRAMOLECULAR PROCESSING

of INFORMATION
MOLECULAR RECOGNITION

The LOCK and the KEY
SPHERICAL SUBSTRATES
The ALKALI METAL CATIONS

A series of spherical species of single charge and increasing size
Selective Binding and Transport of Spherical Cations

SPHERICAL MOLECULAR RECOGNITION
Design of 3D Receptors for Spherical Cations

MACROBICYCLIC CRYPTANDS and CRYPTATES

[2.2.2] CRYPTAND

[2.2.2] CRYPTATE

Structures in the Crystal

1968
CRYPTANDS and CRYPTATES 1968

SPHERICAL RECOGNITION

Complementarity in Size and Shape between Cavity and Cation
TETRAHEDRAL MOLECULAR RECOGNITION

TETRAHEDRAL SUBSTRATE
The AMMONIUM CATION

RECEPTOR with
TETRAHEDRAL RECOGNITION SITE

COMPLEMENTARITY in
SHAPE, SIZE and INTERACTIONS
MACROPOLYCYCLIC STRUCTURES of MOLECULAR RECEPTORS

- Macrocyclic
- Macrotricyclic
- Cylindrical
- Macrobicyclic
- Spherical
ANION RECEPTORS

ANION COORDINATION CHEMISTRY
Supramolecular Catalysis

1) Recognition
2) Reaction
3) Regeneration

1) Substrate binding
2) Structural selectivity for dipeptide esters
3) Large rate accelerations (about 10^4)
4) Saturation kinetics and competitive inhibition
5) High chiral recognition (factor of about 80)

Enzyme Models
MOLECULAR and SUPRAMOLECULAR DEVICES

- SUPRAMOLECULAR OPTICS
- SUPRAMOLECULAR ELECTRONICS
- SUPRAMOLECULAR IONICS
PHOTONIC SUPRAMOLECULAR DEVICE

Double Fonction

\[ \begin{align*}
\text{Light Collection} & : \Sigma A \\
\text{Light Conversion} & : A - ET - E
\end{align*} \]

Processus:
Absorption – Energy Transfer – Emission

Components:
Collector (\( \Sigma A \)) and emitter E

Europium Cryptate

STRONG RED LUMINESCENCE
SUPRAMOLECULAR ELECTRONIC DEVICES

Electron Transfer

Molecular Wire

Charge Separation

Polarized Molecular Wire

D-PS-A  Photodiode

Caroviologene A-A

34 Å

Photoswitch

Caropolyene D-A
Spontaneous but information-controlled generation of supramolecular architectures via molecular recognition patterns.
SELF-ASSEMBLY of the TOBACCO MOSAIC VIRUS

From 2130 protein subunits + 1 molecule of viral RNA
PROGRAMMED CHEMICAL SYSTEMS

MOLECULAR PROGRAMME ↔ SUPRAMOLECULAR OPERATION

INFORMATION stored in the COMPONENTS ↔ PROCESSING via RECOGNITION ALGORITHM defined by the INTERACTION PATTERN

STAGES of INFORMATION INPUT → for SPECIES OUTPUT

RECOGNITION → GROWTH → TERMINATION
INTERMOLECULAR INTERACTIONS
for
SUPRAMOLECULAR SELF-ORGANIZATION

- Electrostatic Interactions
- Hydrogen Bonding
- Donor-Acceptor Interactions
- Van der Waals Forces
- Metal Ion Coordination

+ Medium effects: solvophobic
SELF-ORGANIZATION of METALLOSUPRAMOLECULAR ARCHITECTURES

- BRICKS/COMPONENTS: MOLECULES
- CONNECTIONS / CEMENT: METAL CATIONS

The metal cations process the molecular information in the ligand molecules through the coordination algorithm.
TRINUCLEAR HELICATES

SELF-ASSEMBLY of a TRINUCLEAR DOUBLE HELICAL METAL COMPLEX
SELF-ASSEMBLY of a TRINUCLEAR TRIPLE HELICAL METAL COMPLEX
SELF-ORGANIZATION of METALLOSUPRAMOLECULAR GRIDS

From Nitrogen Ligands with TRIDENTATE Subunits and Metal Cations of OCTAHEDRAL Coordination Geometry

MULTIFUNCTIONALITY
- MULTI-LIGAND
- MULTI-NUCLEAR
- MULTI-METALLIC

ARRAYS of ADDRESSABLE « ION DOTS »
[2x2] GRID ARCHITECTURES
MULTI-FUNCTIONAL SUPRAMOLECULAR DEVICES

★ MULTI-LIGAND
★ MULTI-NUCLEAR
★ MULTI-METALLIC

Supramolecular Electronics
Multiple Redox States
[2x2] [Co\textsuperscript{II}L\textsubscript{4}] Grid

Supramolecular Spintronics
Spin Crossover
Triggered Processes
[2x2] [Fe\textsuperscript{II}L\textsubscript{4}] Grid

Generation of EMERGING PROPERTIES through MULTIPLICITY
[2x2] Grids with Octahedrally Coordinated Metal Ions

Ditopic bis-terdentate ligand

\[ R = H, \text{Me}, \text{Ph} \]

Structure of the \([\text{Co}_4(L)_4]^{8+}\) cation

\[ M = \text{Co}^{\text{II}}, \text{Zn}^{\text{II}}, \text{Ni}^{\text{II}}, \text{Cd}^{\text{II}}, \text{Cu}^{\text{II}}, \text{Pb}^{\text{II}} \]
Multilevel Supramolecular Electronic Species

Reduction of $[\text{Zn}_4\text{L}_4](\text{BF}_4)_8$

« Clustering » of reduction waves

Coulomb Blockade

Ligand:

DMF, TBAPF$_6$ (0.1M), glassy carbon electrode versus ferrocene, room temperature
Multilevel Supramolecular Electronic Species

Electrochemical Reduction of \([\text{Co}_4\text{L}_4](\text{BF}_4)_8\)

INTERNAL COMMUNICATION between the LIGANDS within the GRID mediated by the COBALT CENTERS

DMF, TBAPF$_6$ (0.1M), glassy carbon electrode versus ferrocene, room temperature
[2x2] [Fe₄L₄](ClO₄)₈ Grid: a multiple state magnetic spin transition switch

Three levels

Three triggers

Proton NMR spectroscopy

Angew.Chem.Int.Ed. 2000, 39, 2504-2507
Addressing the Metal Centers in a Supramolecular Electronic Species

The [2x2] Grid \[
[\text{Co}^{II}_4 \text{L}_4](\text{BF}_4)_8
\]

Topography

X Ray Structure

CITS: Current Induced Tunneling Spectroscopy

Lines of 1D ordered \[
[\text{Co}^{II}_4 \text{L}_4]^{8+}
\]

grids on HOPG

Local Resolution of the Co\( ^{II} \) ions

Conductance Transmission Probability
Addressing the Metal Centers of a [2x2] Cobalt(II) GRID

Theory and Experiment

Upper row): 3D representation of DFT-calculated electron density maps within an energy window between $E_F$ and -0.55 eV and between $E_F$ and -1 eV.

(Lower row): Central section of the measured CITS maps.

HOMO of Co$_4$ [2x2]

Electron extraction from the Co-centered HOMO

DFT Calculations
J. Kortus
(MPI Stuttgart)
TOPOSELECTIVE and CHIROSELECTIVE SELF-ASSEMBLY of HETERO-METALLIC [2x2] GRIDS

CHIRAL « CORNER » COMPONENTS

CHIRAL SELECTION in SELF-ASSEMBLY « Coupe de Roi »

[Ru$_2$Fe$_2$] GRID

R

S

Achiral if

Chiral if

Ru$^{II}$

Fe$^{II}$

Cl$^{-}$
SELF-ORGANIZATION of a \([4\times4] \text{Pb}^{\text{II}}_{16}\) GRID Array
from **24 components** : 8 Ligand Molecules and 16 Lead(II) Cations

Single operation
Multiple « hidden » steps

The Pb(II) CENTERS ➞ « ION DOTS »
83 MHz $^{207}$Pb NMR Spectra of the [4x4] Pb$^{II}_{16}$ GRID
NANO-CYLINDERS: CYLINDRICAL NANOSTRUCTURES

3-Dimensional
Nanosize
Cylindrical

Polymetallic
Arrays

by

MULTICOMPONENT SELF-ORGANIZATION
from two different types of ligands
Multilevel/Multicell Metallosupramolecular NANOCYLINDER

\[
\begin{align*}
4 \text{R} & \quad + \quad 3 \text{R} \quad + \quad 12 \text{Cu}^+ \\
\text{R} & \quad = \quad \text{C}_6\text{H}_5
\end{align*}
\]

\[\text{C}_6\text{H}_5 \text{ substituents omitted}\]
NANOCYLINDER

SELF-ORGANIZED
from
3 LINEAR LIGAND MOLECULES
4 PLANAR LIGAND MOLECULES
12 METAL CATIONS Cu(I)
SELF-ORGANIZATION of MULTICOMPARTMENTAL NANOCYLINDERS from

COMPONENTS of THREE TYPES
MULTI-SUBROUTINE SELF-ORGANIZATION

MULTIPLE EXPRESSION of MOLECULAR INFORMATION
SINGLE CODE ↔ SEVERAL OUTPUTS

Processing of the Same Molecular Information through Different Interaction Algorithms

Double Subroutine Process

Metal Cation Coordination Algorithms

linear combination

cross-over

= hexacoordinated ion : Fe(II), Co(II), Ni(II), Cu(II)
= tetracoordinated ion : Cu(I)

= pentacoordinate ion : Cu(II)
= tetracoordinate ion : Cu(I)
Solid State Molecular Structure

- hexacoordinated ion: Fe(II), Co(II), Ni(II), Cu(II)
- pentacoordinated ion: Cu(II)
- tetracoordinated ion: Cu(I)

Solid State Molecular Structure
Are these representations the correct shapes of the free ligands?

NO!

STRONG CONFORMATIONAL PREFERENCE of 2,2’-BIPYRIDINE for the TRANSOID FORM

Induces HELICAL FOLDING of the Molecular Strands
HELICAL FOLDING of a HETEROCYCLIC MOLECULAR STRAND

6 subunits ligand strand

R = SnPr

Solid State Molecular Structure
MOLECULAR SELF-ORGANIZATION through

FOLDING CODONS

FOLDING CONTROL

through

STRUCTURE ENFORCING SUBUNITS

Sequences of Aromatic Heterocyclic Groups

Induction of Superstructures by Intramolecular Self-Organisation of Oligoheterocyclic Strand
Conversion of the β-turn/helicity inducing form of the free pym-py / hyz-pym ligand fragments into an extended linear shape upon binding of a metal ion

**FOLDING / UNFOLDING INTERCONVERSION**

**UNFOLDING by ION BINDING**
Conversion of the β-turn/helicity inducing form of the free pym-py / hyz-pym ligand fragments into an extended linear shape upon binding of a metal ion

**FOLDING by ION BINDING**
Conversion of a linear ligand fragment py-py / hyz-py into a β-turn/helicity inducing form upon binding of a metal cation
MOTIONAL DYNAMIC DEVICES

IONIC MODULATION of EXTENSION/CONTRACTION MOTION

HELICAL STRAND UNFOLDING by ION BINDING
REVERSIBLE IONIC MODULATION of HELICAL STRAND / LINEAR COMPLEX INTERCONVERSION by COUPLING with a COMPETING CRYPTANT LIGAND

HELICAL STRAND UNFOLDING by ION BINDING

[Chemical structures and reaction arrows indicating the process]

Generation of EXTENSION / CONTRACTION MOLECULAR MOTION Fueled by ACID / BASE NEUTRALIZATION ENERGY
MODULATION of COILING / UNCOILING
ION-COUPLLED / pH-INDUCED STRUCTURAL SWITCHING

Sequence of Triggering Agents

Length /Å

38.5 Å

10 Å

Pb(II) [222] H⁺ Base H⁺ Base

Sequence of Triggering Agents
NANOMECHANICAL DEVICES

MOLECULAR

SUPRAMOLECULAR

MOTIONAL DYNAMIC DEVICES

- Molecular/Supramolecular Entities undergoing Triggered Molecular/Supramolecular MOTIONS
- Reversible/Oriented Structural Changes Triggered by External Effectors

Generation of CONTROLLED NANOMECHANICAL MOTIONS between ORGANIZED STRUCTURES
PROGRAMMED SELF-ORGANIZATION

- Spontaneous but controlled generation of well-defined, large, complex, organized, functional supramolecular architectures

- A powerful alternative or complement to NANOFABRICATION and NANOMANIPULATION

From FABRICATION to SELF-FABRICATION

The Ultimate Fabrication!
There's even more room at the top!

COMPLEXITY
the goal is

BEYOND
NANOSCIENCE
and
NANOTECHNOLOGY

There's plenty of room at the bottom!

Richard Feynman
SELF-ORGANIZATION

by DESIGN

by DESIGN

INFORMATION
PROGRAMMATION

with SELECTION

DIVERSITY
DYNAMICS

ADAPTATION
SELF-RECOGNITION in HELICATE SELF-ASSEMBLY

Dynamic Combinatorial Library of Helical Metal Complexes

Dynamic Library of Circular Helicates

Hasenknopf, B. Lehn, J.-M., Kneisel, B.O., Baum, G. Fenske, D. 
SUPRAMOLECULAR CHEMISTRY is a DYNAMIC CHEMISTRY due to the LABILITY / REVERSIBILITY of NON-COVALENT INTERACTIONS enabling CONSTITUTIONAL VARIATION through exchange, incorporation and decorporation of the molecular components of a supramolecular entity.
IMPORT DYNAMICS into MOLECULAR CHEMISTRY through REVERSIBLE COVALENT BONDS

DYNAMIC COVALENT CHEMISTRY

CONSTITUTIONAL DYNAMIC CHEMISTRY BOTH MOLECULAR / COVALENT and SUPRAMOLECULAR / NON-COVALENT

Dynamic Modification of the Constitution of Chemical Entities
CDC

CONSTITUTIONAL DYNAMIC CHEMISTRY

MOLECULAR            SUPRAMOLECULAR

To

SUPRAMOLECULAR CHEMISTRY

From
DYNAMIC CHEMISTRY

- **REACTIONAL**
  - Dynamics of Chemical Reactions

- **MOTIONAL**
  - Molecular Motions
  - Nanomechanical Shape Changes, Motors

- **CONSTITUTIONAL**
  - Dynamic Modification of the Constitution of Chemical Entities

CONSTITUTIONAL DYNAMIC CHEMISTRY
CONSTITUTIONAL DYNAMIC CHEMISTRY

- generates DYNAMIC SUPRAMOLECULAR and MOLECULAR DIVERSITY
- enables the operation of SELECTION

- search for BIOLOGICALLY ACTIVE SUBTANCES
- self-organization of DYNAMIC NANOSTRUCTURES
- development of molecular and supramolecular CONSTITUTIONAL DYNAMIC ASSEMBLIES and MATERIALS
Search for **BIOLOGICALLY ACTIVE SUBSTANCES**

FIND  **THE KEY for THE LOCK**

**DESIGNED CHEMISTRY**

**ONLY ONE KEY : THE RIGHT ONE**

**COMBINATORIAL CHEMISTRY**

**MANY DIFFERENT KEYS, ALL MUST BE TRIED ; ONE OF THEM CAN BE THE RIGHT ONE**

**DYNAMIC COMBINATORIAL / COVALENT CHEMISTRY**

**DCC**

**FRAGMENTS OF KEYS IN CONTINUOUS REARRANGEMENT, ONE OF THE COMBINATIONS, THE BEST ONE, IS SELECTED BY THE LOCK**
Dynamic Search for BIOLOGICALLY ACTIVE SUBSTANCES MOLECULAR RECOGNITION driven COMPONENT SELECTION

VIRTUAL / DYNAMIC COMBINATORIAL LIBRARY

Components

Constituents

Library generation

Library of interchanging species

Initial building blocks
Dynamic Search for BIOLOGICALLY ACTIVE SUBSTANCES
MOLECULAR RECOGNITION driven COMPONENT SELECTION

VIRTUAL / DYNAMIC COMBINATORIAL LIBRARY

**Components**

Library generation

**Initial building blocks**

**Constituents**

Library of interchanging species

**CONSTITUENT EXPRESSION**

Selection of the best binder

**Lock/Key**

The Lock assembles Its Key

Selection by the receptor/lock of the thermodynamically preferred constituent among all the possible combinations/constituents forming the dynamic combinatorial library
**Dynamic Covalent Chemistry (DCC)** implementing reversible reactions

**Amine – Carbonyl Condensations**

- **Imine**
  - $H_2N-R_1 + OHC-R_2 \rightleftharpoons R_1N\equiv R_2 + H_2O$

- **Acylhydrazone**
  - $R_1NCONH-NH_2 + OHC-R_2 \rightleftharpoons R_1N\equiv N\equiv R_2 + H_2O$

- ✓ organic and biological groups
- ✓ compatible with aqueous phase
- ✓ kinetics controllable by pH
CARBONIC ANHYDRASE  Active Site & Inhibitor

\[ \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \]

\[ K_d = 1.1 \text{ nM} \]
A DYNAMIC LIBRARY of IMINES


\[ K_d = 1.1 \text{ nM} \]
EFFECT of CARBONIC ANHYDRASE on LIBRARY COMPOSITION

« DYNAMIC SCREENING »

In absence of Carbonic Anhydrase:
ratio about 1/1 of these two constituents of the dynamic library

In presence of Carbonic Anhydrase:
EXPRESSION / AMPLIFICATION of the LIBRARY CONSTITUENT CLOSEST to the BEST INHIBITOR
Tetrmeric CONCANAVALIN A (Con A) complexed with Trimannoside

J. H. Naismith, R. A. Field
J. Biol. Chem. (1996) 271, 972
Components of a Dynamic Combinatorial Library Directed towards Concanavalin A

Potential generation of 690 constituents
Dynamic Deconvolution of the Concanavalin A Combinatorial Library
DYNAMIC NANOSTRUCTURES

MULTI-COMPONENT SELF-ASSEMBLY of [2x2] GRID ARCHITECTURES from LIGAND SUBUNITS

\[
\begin{array}{c}
\text{2} \quad \text{SO}_3^- \\
\text{NH}_3^+ \\
\text{OH} \\
\text{Ph}
\end{array}
\quad +
\begin{array}{c}
\text{SO}_3^- \\
\text{OH} \\
\text{Ph}
\end{array}
\quad \xrightarrow{\text{Co(II) or Zn(II) + H}_2\text{O}}
\begin{array}{c}
\text{SO}_3^- \\
\text{NH}_3^+ \\
\text{OH} \\
\text{Ph}
\end{array}
\quad +
\begin{array}{c}
\text{SO}_3^- \\
\text{OH} \\
\text{Ph}
\end{array}
\]
DYNAMIC SELECTION of LIGAND COMPONENTS
DRIVEN by FORMATION of a [2x2] GRID COMPLEX

Dynamic Library of Imines

DIVERSITY GENERATION

COMPONENT SELECTION

M = Mn, Fe, Co, Ni, Cu, Zn
CONSTITUTIONAL DYNAMIC MATERIALS

MOLECULAR         SUPRAMOLECULAR

DYNAMERS : Dynamic Polymers

SUPRAMOLECULAR / NON-COVALENT
MOLECULAR / COVALENT
POLYMERIC MATERIALS exhibiting
REVERSIBLE
COMPONENT EXCHANGE

BIODYNAMERS
Dynamic Analogs of Biopolymers
The chemistry of **SUPRAMOLECULAR POLYMERS**

entities generated by

**POLYASSOCIATION** of

COMPLEMENTARY MOLECULAR MONOMERS

through NON-COVALENT INTERACTIONS

controlled by MOLECULAR RECOGNITION PROCESSES

**→ DYNAMIC POLYMERS**
SUPRAMOLECULAR LIQUID CRYSTALLINE POLYMERS

from CHIRAL COMPLEMENTARY H-BONDING MOLECULAR COMPONENTS

\[
\text{TP}_2 + \text{TU}_2 \rightarrow (\text{TP}_2, \text{TU}_2)_n
\]

Tartaric acid spacer \( T = L, D, M \)

\( Z = \text{CH}_3 \quad R = \text{C}_{12}\text{H}_{25} \)

Advanced Materials, 1990, 2, 254
Helical Textures formed by the $LU_2$-$LP_2$, $DU_2$-$DP_2$ and $MU_2$-$MP_2$ strands observed by electron microscopy.
MAIN-CHAIN SUPRAMOLECULAR POLYMER
formed via SEXTUPLE HYDROGEN BONDING
between Molecular Monomers bearing
Complementary Recognition Groups

Cross-linking Monomer
STM Image of a Supramolecular Polymeric Chain at the graphite-solution interface

A + B 6 µmol solution in 1,2,4 trichlorobenzene

Current: 20 pA
Bias: 300 mV

a = 2.51 nm  b = 4.04 nm
A = 5.94 nm²/dimer
α = 35.8°
MOLECULAR / COVALENT DYNAMERS

DYNAMIC POLYMERS generated by POLYCONDENSATION of FUNCTIONAL COMPLEMENTARY MONOMERS through REVERSIBLE COVALENT CONNECTIONS

\[
\text{dialdehyde} + \text{diamine} \rightarrow \text{polyimines}
\]

\[
\text{dialdehyde} + \text{dihydrazide} \rightarrow \text{polyacylhydrazones}
\]
Polyimine DYNAMER FILM

Water-desintegrative film based on a Dynamer containing imine groups
(20 cm x 60 m x 30 µ)

2 tons dynamer prepared

Toward «GREEN» PLASTICS!

T. Nobori et al., Mitsui Chemicals, 2006
MOLECULAR / COVALENT DYNAMERS

POLY ACYL HYDRAZONES

AMIDE

IMINE

REVERSIBILITY

HYDROGEN BONDING

BIOPOLYMERS

DYNAMIC BIOPOLYMERS
BIODYNAMERS
Dynamic Peptoids

MATERIALS

DYNAMIC POLYAMIDES
REVERSIBLE POLYAMIDES
Silicone-derived Covalent Dynamer: **DYNASIL**

![Chemical structures and images of flexible films](image)

Developed by Takashi Ono, Shunsuke FUJII, Mitsui Chemicals Inc.
**MECHANO DYNAMIC POLYMERS**

Soft-to-Hard Transformation of the Mechanical Properties of a Polyacylhydrazone Covalent Dynamer by Incorporation of Monomers

Conversion of a Soft Stretchy Film into a Hard Tough Film by Dynamic Modification

[Chemical structures and images demonstrating the transformation process]
OPTO DYNAMIC POLYMERS
smart optical materials responsive to external stimuli

Color and fluorescence changes of dynamic polymers induced by bond recombination and component exchange

Exchange reaction through the interface of two different dynamic polymers

A-B

A'-B'

A-B

A'-B'

A-B

A'-B'

heated in oven

two dynamic polymer films are superimposed

color and fluorescence changed only where superimposed
**Concept:**
introducing a difference in degree of conjugation by bond recombination

POLYMERS

```
 AB
 [N=N] [N=N]
 [CH] [CH]
```

```
 A'B
 [N=N] [N=N] [C=S] [C=O]
 [CH] [CH] [O] [O]
```

exchange reaction

```
 AB'
 [N=N] [N=N] [C=S] [C=O]
 [CH] [CH] [O] [O]
```

no conjugation

extended local conjugation

weak local conjugation

no conjugation
Can we draw a picture using dynamic polymers? Oui ! bien sûr !

The two polymer films are cut with scissors and superimposed. Both polymer films are formed using a mixed solvent (CHCl3/DMF). Both films are soft and relatively stretchy containing 9-10wt% of DMF.

Color

- yellow color only where superimposed

Fluorescence

- yellow-green fluorescence only where superimposed

Smart optical materials responsive to external stimuli

Both polymer films are heated at 170°C for 5min under 365nm.
Reversible Diels-Alder Reactions
between FULVENES and CYANOOLEFINs
at ROOM TEMPERATURE

$$\text{Dicyanofumarates}$$

$$\text{Alkyl Tricyanoethylene carboxylates}$$

$$\arrow{Self-Contained Dynamic Processes}$$
Formation of a Diels-Alder Dynamer
Self-Healing of Diels-Alder Dynamer Films

Possible Self-Healing Mechanism

Opening of the adducts and chain motion → Formation of new adducts across the interface
ADAPTATION
through
DYNAMIC CONSTITUTIONAL VARIATION
by COMPONENT SELECTION

in response to
☆ environment / medium
☆ phase change
☆ physical effector
☆ chemical effector
☆ morphological change / switching

→ in a CONSTITUTIONAL DYNAMIC NETWORK
Set of CONNECTED INTERCONVERTING CONSTITUENTS
The reversible polycondensation of amphiphilic di(acylhydrazine) and di(aldehyde) monomers gives a dynamic acylhydrazone copolymer, which adopts a helical folded structure to minimize the exposure of hydrophobic surface area (HG groups omitted for clarity).
CONSTITUTIONAL ADAPTATION to the ENVIRONMENT Hydrophobically-Driven Monomer Selection in Dynamers

Competitive Polymerization Uncovers Monomer Component Selectivity

Rigid hydrophobic core

Flexible hydrophilic side-chain

\[ [\text{CA}]_0 = [\text{CH}]_0 = [\text{BH}]_0 = 4.6 \text{ mM in 5 mM aqueous phosphate, 55 °C} \]

Selective polymerization of CH over BH

Selectivity decreases on addition of organic solvent, acetonitrile, to near random at 80% acetonitrile
ADAPTIVE SELF-ASSEMBLY

ADAPTATION to the ENVIRONMENT

Solvent Modulated Reversible Interconversion between Two Self-Assembled Nano-Architectures
Constitutional Dynamic Process
Towards COMPLEX SYSTEMS

CONSTITUTIONAL DYNAMIC NETWORKS

Networks of DYNAMICALLY INTERCONVERTING CONSTITUENTS connected either structurally (molecular and supramolecular arrays) or reactionally (sets of connected reactions or interactions)

PHYSICALLY or CHEMICALLY MODULATED

System of Four Constituents AC, AD, BC, BD from Recombination of four Components A, B, C, D two by two A and B with C and D

AGONISTIC Connectivity

ANTAGONISTIC Connectivity
SELF-ORGANIZATION DRIVEN COMPONENT SELECTION in a SUPRAMOLECULAR G-QUARTET based HYDROGEL formed by Guanosine 5’-Hydrazide

15 mM 22 \degree C pH 4-7 Na\(^+\), K\(^+\), NH\(_4\)^+ 15 mM 22 \degree C

Model of the G-quartets \([G_4-K^+]\) aggregates

TEM picture

Gel in sodium acetate buffer at 15 mM at pH 6
Dynamic Decoration of the G-quartet

DOUBLE DYNAMIC SOL / GEL SYSTEM

★ Supramolecular / non-covalent dynamics ★ Molecular / covalent dynamics

Dynamic Decoration of the G-quartet

Formation of a SOL or a GEL depending on the residue attached at 15 mM concentration
Dynamic Covalent / Combinatorial Library

\[
\begin{align*}
A & : \text{AcHN} - \text{CO} - \text{NH} - \text{NH}_2 \\
B & : \text{AcHN} - \text{CO} - \text{NH} - \text{NH}_2 - \text{OH} \\
C & : \text{HO} - \text{C} - \text{O} - \text{C} - \text{P} - \text{O} - \text{OH} \\
D & : \text{HO} - \text{C} - \text{O} - \text{SO}_3 - \text{Na} \\
\end{align*}
\]

\[\text{pD 6} \quad 1:1:1:1\]

15 mM each in 0.5 M sodium acetate buffer

\[\begin{align*}
\text{AD} & : \text{AcHN} - \text{CO} - \text{NH} - \text{N}\text{N} - \text{N} - \text{C} - \text{S} - \text{Na} - \text{SO}_3 \\
\text{AC} & : \text{AcHN} - \text{CO} - \text{NH} - \text{N}\text{N} - \text{N} - \text{C} - \text{S} - \text{Na} - \text{HO} - \text{P} - \text{O} - \text{OH} \\
\text{BD} & : \text{AcHN} - \text{CO} - \text{NH} - \text{N}\text{N} - \text{N} - \text{C} - \text{S} - \text{Na} - \text{SO}_3 \\
\text{BC} & : \text{AcHN} - \text{CO} - \text{NH} - \text{N}\text{N} - \text{N} - \text{C} - \text{S} - \text{Na} - \text{HO} - \text{P} - \text{O} - \text{OH} \\
\end{align*}\]

Statistical distribution

\text{NO SELECTION}

as there is no gel formation with these constituents.
Self-Organization-driven Dynamic Component Selection through Gel Formation

Amplification of constituent B leading to formation of a stronger gel

SELECTION under SELF-ORGANIZATION PRESSURE

Significance for PREBIOTIC EVOLUTION of MATTER

Towards COMPLEX SYSTEMS

CONSTITUTIONAL DYNAMIC NETWORKS

Networks of DYNAMICALLY INTERCONVERTING CONSTITUENTS connected either structurally (molecular and supramolecular arrays) or reactionally (sets of connected reactions or interactions)

PHYSICALLY or CHEMICALLY MODULATED

System of Four Constituents
AC, AD, BC, BD
from Recombination of
four Components A,B,C,D
two by two A and B with C and D

AGONISTIC Connectivity
ANTAGONISTIC Connectivity

AC --- AD
|    |
|    |
|    |
|    |
BC --- BD
|    |
|    |
|    |
|    |
CONSTITUTIONAL DYNAMIC NETWORKS

PHYSICALLY or CHEMICALLY MODULATED

Inorganized State
Statistical Distribution

Organized State
Enforced Distribution

Organization
Organized Phase
Gel formation

AC, BD = agonists
AC, BD antagonists to AD and BC

AC, BD antagonists to AD and BC

SELECTED
driven by
SELF-ORGANIZATION

ADAPTATION

AGONISTIC Connectivity

ANTAGONISTIC Connectivity

AMPLIFICATION of AC / BD
CONSTITUTIONAL DYNAMIC CHEMISTRY

MOLECULAR

CONSTITUTIONAL DYNAMIC MATERIALS DYNAMATS

SUPRAMOLECULAR

ADAPTIVE MATERIALS

ADAPTIVE TECHNOLOGIES
CONSTITUTIONAL DYNAMIC CHEMISTRY

MOLECULAR

DYNAMIC CONSTITUTIONAL DIVERSITY

SUPRAMOLECULAR

- chemical systems undergoing continuous recomposition/recombination/reorganization deconstruction/reconstruction
- responding under the pressure of internal external factors / stimuli
- through constitutional variation

Novel Paradigm: **SELECTION** through Dynamic Constitutional Diversity responding to the pressure of internal/external factors

**ADAPTATION**
MOLECULAR CHEMISTRY

CONSTITUTIONAL DYNAMIC CHEMISTRY

SELF-ORGANISATION

DESIGN

MOLECULAR CHEMISTRY

DIVERSITY GENERATION

SELECTION

CONSTITUTIONAL DYNAMIC CHEMISTRY

ADAPTIVE CHEMISTRY

SUPRAMOLECULAR CHEMISTRY

DYNAMICS

Towards

ADAPTIVE EVOLUTIVE DARWINIAN CHEMISTRY

TOWARDS
SELF-ORGANIZATION

Steps towards COMPLEX MATTER

DESCRIBE THE PROCESSES THAT LED TO OCCUR IN

UNDERSTAND

CREATE NOVEL FORMS/EXPRESSIONS OF COMPLEX MATTER

ORGANIZED – LIVING – THINKING MATTER!